The effect of GABRB3 polymorphisms on brain function and structure in healthy male volunteers assessed by multimodal imaging

Abstract

The combination of genetic information and data provided by magnetic resonance imaging (MRI) techniques is commonly referred as *imaging genetics*, an interesting approach with the potential to investigate the mechanisms linked to genetic variation. The gene that codifies the beta–3 subunit of the GABA-A receptor (GABRB3) is of great interest due to its early expression during embryonic stages, its role in neurodevelopment and its relationship with neurologic diseases such as epilepsy and autism. In order to investigate the possible effects of GABRB3 on brain structure and function, a sample of 63 healthy young male volunteers was measured using multimodal imaging techniques including: structural imaging, diffusion-weighted imaging, resting state fMRI, magnetic resonance spectroscopy and electroencephalography (EEG). Inter-group differences in brain function and structure were tested on the basis of frequency and prevalence of G2, the most frequent allele of GABRB3 in the population. The results showed that there were significant differences in diffusion parameters among the different subgroups on the basis of the G2 allelic prevalence and frequency. Non-carrier volunteers exhibited significantly increased axial diffusivity in the right superior longitudinal fasciculus, right corticospinal tract and body of the corpus callosum compared to homozygote carriers of the G2 allele. Initially, such differences in diffusion parameters were only evident for axial diffusivity, although when a focused region-of-interest analysis was performed, differences in fractional anisotropy and mean diffusivity emerged. A statistically significant higher *delta* voltage in the global activity of EEG was also found in homozygote carriers of the G2 allele compared to heterozygote carries. The results presented here confirm the importance of the expression of GABRB3 gene in brain structure, particularly in defining the features of the white matter microstructure. Differences in EEG were also found to depend on the frequency of the G2 allele, which confirms the conclusions of previous investigations in which the expression of GABRB3 was crucial for the activity of EEG.